REMARKS

This is a response to the Office Action mailed June 30, 2003. Claims 1-6, 11-13 , 21, 22, 24, 27 and 29-50 are pending in the application. Claims 1-6, 11-13 , 21, 22, 24, 25[1], 27 and 29-39 have been rejected by the Examiner. As noted above, Applicants have amended Claims 1, 11, 33 and 39 and submitted new Claims 40-50. The amendments and the new Claims 40-50 are fully supported by the written description. Also, no new matter has been introduced into the application.

Claim Rejections – 35 U.S.C. § 103

The Examiner has rejected Claims 1-6, 11-13, 21, 22, 24, 25, 27 and 29-39 under 35 U.S.C. §103(a) as being unpatentable over Roth et al. (USPN 5,837,313). Roth et al. is directed to a method of delivering bioactive molecules to cells. Roth et al. disclose that "encapsulation of nucleic acid molecules or biologically active proteins within biodegradable, biocompatible polymeric microparticles which are appropriate sized to infiltrate, but remain trapped within, the capillary beds and alveoli of the lungs can be used for targeted delivery to these regions of the body following administration to a patient by infusion or injection" (abstract).

1. CLAIMS 1-6 AND 11-13.

In order to establish *prima facie* obviousness, **all of the claimed limitations must be taught or suggested** in the references cited. Roth et al. clearly fail to disclose a method of achieving a therapeutic effect that includes

> delivering a particle containing **a therapeutic substance and a disintegrant** to an anatomical structure comprising a lumen such that said particle forms an embolus within said lumen for a transitory period, **said transitory period being less than seven days and less than the duration which results in cell damage or cell death**; and
>
> wherein said therapeutic substance is released from said particle, causing said therapeutic effect

[1] Applicants note that Claim 25 was not originally presented with the application as filed, and is therefore not pending.

as recited by amended Claim 1.

Moreover, Roth et al. fail to disclose all of the limitations of amended Claim 11, such as a method that includes

> delivering a particle comprised of **a disintegrant and a therapeutic substance** to an anatomical structure including a lumen, said particle having a first diameter sufficient to form an embolus within said lumen at a first site; **wherein said disintegrant is capable of causing said particle to degrade within said lumen to a second diameter smaller than the diameter of said lumen at said first site in less than seven days to release said particle from said first site to mitigate or prevent cellular damage at said first site.**

Roth et al. fail to disclose that their microparticles contain **a therapeutic substance and a *disintegrant***, and are capable of forming emboli for a duration that is less than the duration which results in cell damage or cell death. There is absolutely no disclosure in Roth et al. directed to producing microparticles by specifically combining a therapeutic substance with a disintegrant (e.g., croscarmellose, povidone, lactose, or mannose) so that the particles will rapidly disintegrate into fragments to achieve a therapeutic benefit which is different than the benefit pursued by Roth et al.

Additionally, there would have been no suggestion or motivation to modify the Roth et al. microparticles by combining a therapeutic substance with a disintegrant. First, Roth et al. do not recognize the problem of cellular damage caused by microparticles that are lodged in the lumen for a duration which results in cell damage or cell death. Instead, Roth et al. teach that the microparticles can be lodged for as long as **six months** (col. 4, line 38). This extremely long duration suggested by Roth et al. clearly teaches away from combining a therapeutic substance with a disintegrant. Applicants respectfully request the Examiner to remove the rejection and allow the claims.

2. CLAIMS 21-31.

Roth et al. also do not suggest or disclose a method of achieving a therapeutic effect within an anatomical structure having a first region and a second region, said second region

being located downstream of said first region and having a smaller cross-sectional diameter than said first region, where the method comprises

> delivering a particle having a first size in which said particle is not capable of passing from said first region into said second region, **said particle comprising a water soluble polymer and a hydrophobic counterion**; and
>
> wherein said particle subsequently reduces from said first size to a smaller second size as said particle travels through said anatomical structure, allowing said particle to pass into said second region

as recited by Claim 21. In particular, Roth et al. at least do not disclose "delivering a particle having a first size in which said particle is not capable of passing from said first region into said second region, **said particle comprising a water soluble polymer and a hydrophobic counterion.**"

In the Examiner's Office Action dated June 30, 2003, the Examiner completely failed to address the limitations of independent Claim 21, and dependent Claims 22, 24, 27 and 29-31. Applicants respectfully request the Examiner to identify where in the Roth et al. reference it is disclosed that the microparticles are formed by specifically combining **a water soluble polymer and a hydrophobic counterion.** Otherwise, please allow the claims.

3. CLAIMS 32 AND 33

Roth et al. also do not suggest or disclose all of the limitations of Claim 32 such as "delivering a particle comprised of **a biodegradable compressed material and a therapeutic substance** to a lumen, said particle having a first diameter sufficient to form an embolus within said lumen at a first site." As above, in the Examiner's Office Action, the Examiner completely failed to address the limitations of Claim 32. Applicants respectfully request the Examiner to identify where in the Roth et al. reference it is disclosed that the microparticles are formed by specifically combining **a biodegradable compressed material and a therapeutic substance.** Otherwise, please allow the claims.

4. CLAIMS 34-39

It is also clear that Roth et al. do not disclose all of the limitations of Claims 34-39. For instance, Roth et al. do not disclose all of the limitations of Claim 34, such as a method of delivering a therapeutic substance to a lumen network including

> **occluding a portion of said lumen network**; and
> delivering a particle to a lumen in said lumen network upstream of said occlusion, the particle comprising a biodegradable substance, **wherein said occlusion prevents said particle from entering said portion of said lumen network.**

It is the Examiner's position that the

> purpose of the Roth disclosure is to deliver biologically active agents to a targeted site in the vascular system wherever treatment is needed. Furthermore, Roth et al. achieve the same result as that sought by applicant, which is the vascularization or [sic] the targeted area. Absent evidence to the contrary, it appears that the particulars as to whether the microparticles are introduced below or above the occlusion does not render patentable distinction to the claim. Any evidence provided to rebut this statement must be shown to depend solely on the actual placement of the microparticles with respect to the occlusion.

From the Examiner's comments, it appears that the Examiner is missing an important distinction between the Roth et al. reference, and the claims directed to the placement of the particles. In particular, it appears that the Examiner has missed the fact that the Roth et al. fail to disclose or even suggest the <u>specific action</u> **of occluding a portion of a lumen network**. Although Roth et al. suggest that the microparticles can be administered by a catheter having occluding balloons (see, col. 13, lines 61-64), Roth et al. do not recognize that a portion of the artery should be occluded before injecting the microparticles in order to direct the microparticles away from the occluded portion. Instead, Roth et al. merely disclose that the occuluding balloon can be useful to aid in the separation of a polymer coating from the balloons (see., col. 14, lines 1-4). For vascularization treatments, Roth et al. teach that the particles should be injected "into the artery feeding the affected limb or region" (col. 14, lines 38-39). The method of Roth et al., therefore, allows the microparticles that are injected to travel haphazardly through the artery as propelled by the blood flow without being directed to a particular target lumen. In short, Roth et

al. can be distinguished from the present invention because Roth et al. clearly do not disclose occluding a section of the lumen. This is a very important distinction because otherwise the microparticles can be propelled to unwanted regions of the body.

Accordingly, the Applicants respectfully request that the Examiner reconsider the finding of obviousness, and allow independent Claims 34 and 35. Claims 36-39 depend directly on Claim 35, and should be allowable for at least the same reason.

CONCLUSION

Applicants request an interview with the Examiner after submission of this Response. Applicants also respectfully request the Supervisory Patent Examiner to be present for the Examiner Interview.

Claims 1-6, 11-13, 21, 22, 24, 27 and 29-50 are pending in this application. Examination and allowance of the claims are respectfully requested. If the Examiner has any questions or concerns, the Examiner is invited to telephone the undersigned attorney at (415) 954-0345.

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